PATENT

Docket No. 4007528/173387

CERTIFICATE OF EFS ELECTRONIC TRANSMISSION

I hereby certify that this paper is being transmitted to the United States Patent and Trademark Office by the USPTO EFS web electronic filing system on November 13, 2009.

/Holly D. Kozlowski/

Holly D. Kozlowski

IN THE UNITED STATES PATENT & TRADEMARK OFFICE

Applicant:	Sabine Stumvoll et al	:	Confirmation No.: 1495
Serial No.:	10/027,625	:	Group Art Unit: 1644
Filing Date:	December 21, 2001	:	Examiner: Nora M. Rooney

For: **Use of a Pure Allergen Component**

REPLY BRIEF

Mail Stop Appeal Brief - Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

The present Reply Brief is submitted in response to the Examiner's Answer which was mailed from the U.S. Patent and Trademark Office on September 14, 2009 (Appellants note that while the Examiner's Answer title page bears a "Mailed Sep 11 2009 Group 1600" indication, the actual Transmittal for the Examiner's Answer bears a "Mail Date" of September 14, 2009 (9/14/2009), as shown in the Image File Wrapper (IFW)).

This Reply Brief particularly replies to new arguments which are set forth in the Examiner's Answer but not otherwise found in the prosecution history.

A. The Examiner Asserts that the Method Does Not Achieve More Accurate Identification

Beginning at page 11 of the Official Action, the Examiner for the first time asserts that the claimed method "does not more accurately identify an individual as being *Parietaria* allergic." The

Examiner quotes a portion of the specification at page 1, lines 12-19 and refers to the specification at page 2, lines 1-6 as disclosing "that allergic cross-reactivity to other allergens may elicit allergic symptoms and be clinically relevant." The Examiner asserts that the "information that Par j 1 does not cross react with other allergens that are not in the *Parietaria* species does not distinguish this method over that of the prior art, nor does it more accurately identify an individual as being *Parietaria* allergic", and the recited method and that of EP 707 065 A2 (EP '065) "are directed to using Par j 1 allergens to diagnose individuals with allergies to *Parietaria.*" Further, the Examiner asserts that Appellants' arguments that the prior art does not teach the use of any of the proteins or peptides as reagents to distinguish between genuine *Parietaria* pollen sensitization and cross-reaction-mediated seropositivity to *Parietaria* pollen extract are directed to limitations that are not present in the claims.

The Examiner's comments indicate a failure to consider the presented claim limitations.

The present invention is directed to methods for serologically identifying with improved accuracy an individual known to be weed pollen allergic as *Parietaria*. It is important to determine the allergen which triggers an allergic reaction in an individual in order to allow the individual to avoid the allergen and/or to allow selection of an appropriate treatment of the allergic disease and, particularly, to allow selection of an appropriate allergen extract for immunotherapy. To understand the importance of the present method, it is necessary to recognize that some allergens, for example in any particular weed species, have structurally similar homologs in other species and therefore show serological cross-reactivity, but the serological cross-reactivity may or may not be capable of eliciting an allergic symptom. This means that in serological testing using allergen extract, an individual serum sample may test positive for a particular species, yet the signal is a false positive as it represents reaction of an antibody with a cross reactive homolog which does not elicit an allergic symptom. The methods of the present invention are based on the discovery that Par j 1 and

Par j 2, as pure allergens, have little or no cross reactivity so that a positive response in serological testing with Par j 1 and Par j 2 represents a true positive diagnosis.

The extent to which such false positives are problematic with respect to *Parietaria* is demonstrated in the present specification. Specifically, the inventors show that in a test group of patients from Austria (n=42), Scandinavia (n=8), the U.S. (n=18), and Italy (n=37), almost all patients contained IgE antibodies to *Parietaria* pollen extracts (i.e. not pure components). However, only a few Austrian (4) and no Scandinavian or US patients' sera had IgE that bound to Par j 2 (i.e., to the pure component). Thus, patient samples which showed a positive response to *Parietaria* pollen extracts but not to Par j 2 may be false positives. The ability to eliminate *Parietaria* as the causative allergen source for these patients avoids unnecessary and ineffective treatments which would be based on a false *Parietaria* positive test. On the other hand, for the individuals whose serological testing was positive for Par j 2, these individuals are accurately diagnosed and therefore effective treatment based on the accurate positive *Parietaria* testing can be implemented. As set forth in the specification, selection of an appropriate allergen source for immunotherapy which accurately reflects the primary or actual sensitizer is highly desirable with respect to treatment efficacy, risk of acute side effects and induced additional sensitization, as well as with respect to cost savings and reduced inconvenience to patients. Thus, contrary to the Examiner's assertion, the presently claimed methods do more accurately identify an individual as being *Parietaria* allergic.

Moreover, claim 30 recites a step of "selecting a pure *Parietaria* allergen component known to have limited or no cross-reactivity" and a subsequent step of "contacting serum from the selected individual with the pure allergen component, wherein the pure allergen component is pure Par j 1 or Par j 2 allergen component." As such, contrary to the Examiner's assertion, the present claims do contain the limitation that the proteins or peptides as reagents distinguish between genuine

Parietaria pollen sensitization and cross-reaction-mediated seropositivity to *Parietaria* pollen extract. More importantly, however, as the limited or no cross-reactivity is a known property in the present methods, the ability to accurately identify *Parietaria* allergy according to the present methods, rather than identifying a false positive, is achieved.

B. The Examiner Asserts that Appellants are Relying on a Previously Unappreciated Property

At page 12 of the Examiner's Answer, the Examiner asserts that Appellants are attempting to rely on a previously unappreciated property of the allergen used in the method in order to make the method patentably distinct, cross-reactivity is an inherent property, and there are no active steps that make the method different than that of the prior art.

Again, the Examiner's comments indicate a failure to consider the presented claim limitations.

The present invention does not claim Par j 1 or Par j 2 as new. However, what the Appellants have discovered as new and undisclosed, recognized or suggested in the prior art, is that Par j 1 and Par j 2, as pure allergens, have little or no cross reactivity, and Appellants claim a new process taking advantage of this property. It is well settled that the discovery of a new use for an old structure based on unknown properties of the structure might be patentable to the discoverer as a process of using, *In re Hack*, 245 F.2d 246, 248 (CCPA 1957) and MPEP 2112.02. The presently claimed methods recite a unique combination of steps that are not disclosed in EP '065 and the benefit of which is not disclosed, suggested or recognized in EP '065.

According to claim 30, the method comprises first selecting an individual known to be weed pollen allergic, wherein it is not known if the individual is *Parietaria* allergic. The Examiner has not indicated any disclosure in EP '065, and Appellants find no disclosure in EP '065, of a method which includes a step of selecting an individual known to be weed pollen allergic, wherein it is not

known if the individual is *Parietaria* allergic. To the contrary, as noted in Appellants' Appeal Brief, in Example 8 relied upon by the Examiner, EP '065 employs "**pools of sera**" (page 11, line 56, emphasis added) from Italy (a pool of 13 sera) and Canada (a pool of 7 sera). One of ordinary skill will appreciate that using pooled sera does not provide any diagnostic value relative to an individual and particularly does not comprise first selecting an individual known to be weed pollen allergic, wherein it is not known if the individual is *Parietaria* allergic.

At page 13 of the Examiner's Answer, the Examiner asserts that "the diagnostic method may be performed using pooled serum of individuals who are weed pollen allergic, but not Parietaria allergic and it would provide diagnostic value to all individuals in pooled serum." First, it is important to note that the present method does not relate to a method of diagnosing a pool of individuals as non *Parietaria* allergic. To the contrary, the method of claim 30 is for serologically identifying with improved accuracy an individual known to be weed pollen allergic as *Parietaria* allergic, and comprises, inter alia, identifying a specified individual as *Parietaria* allergic if the contacted serum contains IgE binding to said pure allergen component. Neither the limitations of the preamble of claim 30 nor the limitations of this final step of claim 30 are met by the Examiner's scenario.

Further, claim 30 recites the steps of selecting a pure *Parietaria* allergen component known to have limited or no cross-reactivity and contacting serum from the selected individual with the pure allergen component, wherein the pure allergen component is pure Par j 1 or Par j 2 allergen component. The Examiner has not indicated any specific disclosure in EP '065, and Appellants find no specific disclosure in EP '065, of a method which includes such steps. To the contrary, EP '065 discloses in the "Immunoassay" discussion at page 7, lines 5-31, that a **mixture** of peptides may be used either as an immunogen in a composition or as a diagnostic agent (emphasis added), thereby demonstrating the EP '065 does not contemplate the diagnostic use of a pure *Parietaria* allergen

component, particularly a pure *Parietaria* allergen component known to have limited or no cross-reactivity, as compared with mixtures of *Parietaria* allergen components having cross-reactivity, to distinguish between general weed pollen allergy and *Parietaria* allergy. Similarly, EP '065's Example 8 relied upon by the Examiner does not indicate that a pure *Parietaria* allergen component known to have limited or no cross-reactivity is employed so that the presence of IgE identifies an individual as *Parietaria* allergic, rather than exhibiting cross-reactivity to one or more *Parietaria* allergens. To the contrary, EP '065 discloses that western blot analysis "**of *Parietaria* protein extracts**" (page 11, lines 55-56, emphasis added) was conducted. Thus, Example 8 employed extracts, not a pure allergen component. As discussed above, the use of an extract fails to distinguish between false positive and accurate positive *Parietaria* results. EP '065's use of *Parietaria* protein extracts in Example 8 underscores the lack of recognition by EP '065 of the importance of a method as recited in claim 30 employing the recited pure allergen component of limited or no cross reactivity to accurately identify *Parietaria* allergy.

The Examiner also referred to page 4, lines 41-47 of EP '065, which passage merely indicates that a diagnostic procedure comprises contacting serum from an individual with the recombinant protein or peptide and determining the formation of a complex between the recombinant protein or peptide and pollen specific antibodies in the serum. However, Appellants find no elaboration of this disclosure anywhere in the remainder of EP '065 other than in the immunoassay discussion at page 7 which employs a mixture of peptides as a diagnostic agent. Moreover, there is no teaching, suggestion or recognition that Par j 1 or Par j 2 as a pure allergen component is used as recited in claim 30. Further, EP '065 fails to teach or suggest use of Par j 1 or Par j 2 as a pure allergen component in a method as presently claimed in diagnosing an individual known to be weed pollen allergic wherein it is not known if the individual is *Parietaria* allergic, as *Parietaria* allergic with improved accuracy.

Finally, claim 30 recites the steps of determining the presence of IgE binding to said pure Par j 1 or Par j 2 allergen component and identifying the individual as *Parietaria* allergic if the contacted serum contains IgE binding to said pure allergen component. As EP '065 does not disclose any step employing a serum sample from an individual known to be weed pollen allergic, wherein it is not known if the individual is *Parietaria* allergic, or any step of contacting such a sample with a pure *Parietaria* allergen component known to have limited or no cross-reactivity, particularly with Par j 1 or Par j 2, EP '065 does not teach any method which includes a step of identifying such individual as *Parietaria* allergic if the contacted serum contains IgE binding to said pure allergen component.

Accordingly, the Examiner's assertion that there are no active steps that make the method of claim 30 different than that of the prior art is clearly in error.

The failure of the Examiner to focus on the limitations of claim 30 is highlighted in the first paragraph of page 13 of the Examiner's Answer which states "the diagnostic method is generally taught in the reference, so there is no requirement that the use of pooled serum samples in the reference provide the only support for the recited method." Anticipation is not established by asserting the claimed method is "generally taught" so the specific claim limitations may be ignored. Rather, anticipation under 35 U.S.C. §102 requires that each and every element as set forth in the claims is found, either expressly or inherently described, in a single prior art reference, *In re Robertson*, 49 U.S.P.Q. 2d 1949, 1950 (Fed. Cir. 1999). The Examiner has not shown that each and every element as set forth in claim 30 is described, either expressly or inherently, in EP '065, but rather merely has established that EP '065 discloses recombinant *Parietaria* proteins and derived peptides.

C. The Examiner Newly Relies on In re Cruciferous Sprout Litigation

At page 12 of the Examiner's Answer, the Examiner newly cites *In re Cruciferous Sprout Litigation*, 301 F.3d 1343 (Fed. Cir. 2002) as supporting the Examiner's rejection. However, *In re Cruciferous Sprout Litigation* is easily distinguished from the present facts and issue. That is, in *In re Cruciferous Sprout Litigation*, the patentee relied predominantly on the claim preambles as distinguishing the claimed methods from the prior art and did not establish any difference in the steps of the claimed methods. In contrast, as discussed above and in detail in Appellants' Appeal Brief, EP '065 fails to disclose numerous limitations in the recited steps of claim 30, in addition to failing to disclose the limitations of the preamble of claim 30. Thus, the Examiner's reliance on *In re Cruciferous Sprout Litigation*, is misplaced and not relevant to the determination of patentability of claim 30.

D. Conclusions

For the reasons set forth in detail in the Appeal Brief and the additional reasons set forth above, claims 30-36 are neither anticipated by EP '065 nor rendered obvious over EP '065 in view of Duro et al. While each of these cited references identifies recombinant *Parietaria* proteins, neither of these references teaches or suggests a method as recited in claim 30 for serologically identifying with improved accuracy an individual known to be weed pollen allergic as *Parietaria* allergic, and comprising, inter alia, contacting serum from a selected individual known to be weed pollen allergic, wherein it is not known if the individual is *Parietaria* allergic, with a pure allergen component known to have limited or no cross-reactivity, wherein the pure allergen component is pure Par j 1 or Par j 2 allergen component. Additionally, neither of these references, alone or in combination, teach, suggest or recognize that such a method eliminates false positive identifications for *Parietaria* allergy. Accordingly, the rejections under 35 U.S.C. §§102 and 103 should be reversed. Favorable action by the Board is respectfully requested.

Respectfully submitted,

/Holly D. Kozlowski/

Holly D. Kozlowski, Reg. No. 30,468
Porter, Wright, Morris & Arthur LLP
250 East Fifth Street, Suite 2200
Cincinnati, Ohio 45202
(513) 369-4224